Annals of Clinical and Analytical Medicine
Original Research

Development of the corpus callosum during normal growth

Development of the corpus callosum

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Abstract

Aim: Corpus callosum is the main structure communicating between the two brain hemispheres. This study aimed to investigate the differences in the corpus callosum's and cranium's shape during growth and assess their potential clinical implications.

Material and Methods: Cranium and corpus callosum shape data were collected from two-dimensional digital images. Generalized Procrustes analysis was used to obtain mean shapes between consecutive age groups. Shape deformation of the corpus callosum between successive age groups was evaluated using the thin-plate spline method.

Results: There were significant age-based differences were in the corpus callosum and cranium shape. The most prominent deformation was seen in the posterior midbody (a corpus callosum region), while the cranium deformation was observed in the biparietal area. There were significant differences in corpus callosum shape between 1- and 2-year age groups. The diameter of the cranium increased up to the age of 4 years; however, this increase was not uniform, especially in the biparietal areas.

Discussion: The skull's growth and the corpus callosum's development are not similar. The development of the corpus callosum may be a better indicator of neural development than skull enlargement.

Keywords

Corpus Callosum, Cognition, Development, Shape Analyses, Skull

DOI: 10.4328/ACAM.21812 Received: 2023-07-07 Accepted: 2023-08-14 Published Online: 2023-08-18 Printed: 2023-09-01 Ann Clin Anal Med 2023;14(9):844-848

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This study was approved by the Ethics Committee of Bursa Uludag University (Date: 2019-12-25, No: 2019-21/17)

Introduction

The corpus callosum is a thick bundle of nerve fibers that divides the cerebral cortex lobes into left and right hemispheres and provides connectivity between the right and left sides of the brain. It contains approximately 200 million axons symmetrically distributed to the frontal, parietal, temporal, and occipital lobes [1]. The corpus callosum transfers motor, sensory, and cognitive information between the hemispheres. Many studies have investigated the relationship of the shape of the corpus callosum with gender, race, hand dominance, behaviors, diseases, and developmental abnormalities [2,3].

Morphometrics is a field concerned with the study of variations and changes in the size and shape of organisms or their structures. It can also be defined as the quantitative analysis of a biological form [4,5]. Statistical shape analysis is a modern geometric morphometric analysis method that uses the shape of organs or organisms as input data. This entails analysis of the changes in the shape of the biological structure of interest by using anatomically significant points called landmarks. This analysis can unravel the changes in the structure's shape linked to demographic factors, environmental factors, or disease. This quantitative analysis also enables the interpretation of shape differences and potential general or localized deformations in the target structure or organ. Many recent health-related studies have revealed that statistical shape analysis can be used as a supportive analysis type alongside the existing imaging techniques [6,7].

This study aimed to investigate the differences in the shape of the corpus callosum and cranium during the growth period in early childhood and to explore their potential clinical implications.

Material and Methods

Patient Selection

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Bursa Uludag University IRC (2019-21/17).

In this study, we retrospectively used midline sagittal magnetic resonance images and axial cranial magnetic resonance images passing through the level of the foramen of Monroe of 30 patients in the age group of 1–5 years. Previously reported normal Magnetic resonance imaging (MRI) scans were obtained from the archives of Bursa Uludag University. MRI was performed in a 3.0-Tesla MRI Device (Achieva, Philips, Best, Netherlands). Informed consent was obtained from the legal guardians of all participants, and the university ethics committee approved this retrospective study and the study protocol.

Obtaining 2D Landmarks

An expert radiologist selected the sagittal midsections that most clearly displayed the cerebral aqueduct, corpus callosum, and superior colliculus manually from the sagittal planes. The anterior-posterior commissure line and the inter-hemispheric fissure were identified and used to align the brain of all subjects to a standard position. Statistical shape analysis was performed to evaluate the corpus callosum shape using 16 homologous landmarks (Figure 1) used in previous studies [8]. We also implemented statistical shape analysis of the cranium using homologous anatomical landmarks (Figure 1) used in a previous study [3].

The descriptions of these landmarks are provided in Table 1.

Collection of Two-Dimensional Cranial Landmarks

The landmarks were chosen based on reliability, maximizing anatomical coverage, and cranial morphological descriptions. Corpus callosum and cranial data were collected from two-dimensional digital images. Standard anatomic landmarks were selected and marked on each digital image using the tpsDig2software [Rohlf F: TpsDig, ver. 2.04. Department of Ecology and Evolution, the State University of New York. Stony Brook. 2005.]. The landmark reliability was evaluated using the intrarater reliability coefficient, calculated with a two-facet crossed design ('landmark pairs-by-rater-by-subject,' l x r x s) [9]. The landmarks were marked for all images by an investigator. For calculating the "G" reliability coefficient, 30 images were randomly selected and marked. The same investigator marked the same landmarks on these images two weeks after the first marks. The G coefficient calculated showed strong repeatability (G = 0.9768). Landmark reliability calculations were performed from the following link: http://biostat.home.uludag.edu.tr/landmark_reliability/G_coefficient.html

Geometric Morphometric Analysis

Differences in the shape of the corpus callosum and cranium between consecutive age groups were assessed by performing a Generalized Procrustes analysis. Box's M procedure was used to test the equality of variance–covariance matrixes. If the variance–covariance matrixes were unequal ($p<0.05$), the James FJ test based on a resampling procedure was performed; otherwise, the Hotelling T2 test based on a resampling procedure was considered [1]. Procrustes' mean shapes were calculated for thin-plate spline (TPS) analysis, derived from a mathematical model used in computer graphics and applied to morphometrics by Bookstein [10]. The primary purpose of TPS is to compare two different shapes by deforming one mean shape to the other. The points exhibiting the greatest enlargements or reductions, labeled as deformations, were established through the TPS analysis [11].

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

There was no significant difference between age groups concerning gender distribution ($p=0.518$). The average corpus callosum shapes of the various age groups are shown in Figure 2.

In the analyzes performed between consecutive age groups, there were significant differences in the corpus callosum shapes between children in the 1-year-old and 2-year-old groups ($p=0.040$). However, there were no significant differences in this respect between the two-year-old and three-year-old groups, between three-year-old and four-year-old groups, and between four-year-old and five-year-old groups ($p=0.129$, $p=0.862$, and $p=0.391$, respectively). TPS analysis was also performed using mean corpus callosum shapes of one-year-old and two-year-old groups obtained from the Procrustes analysis. The TPS graphic shows the high level of deformations in corpus callosum shapes from one year to two years (Figure 2). The most significant deformation was observed between the age of 1 to 2 years,

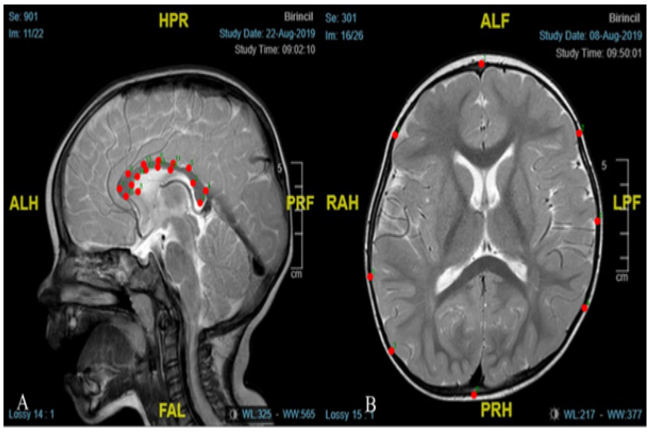

Figure 1. A) T1-weighted mid-sagittal slice demonstrating the corpus callosum landmarks; B) Landmark markings on the cranium.

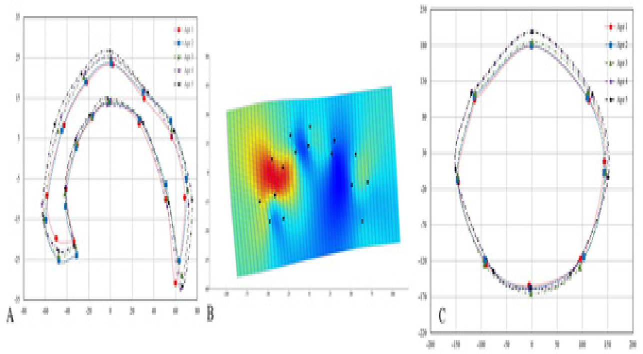

Figure 2. A) Procrustes' mean shapes for the corpus callosum images in various age groups; B) A thin-plate spline demonstrating the mean corpus callosum shape deformation from the age of 1 to 2 years. The expansion factors at the landmarks are shown with colors. C) Procrustes mean shapes for the cranium images of age-groups.

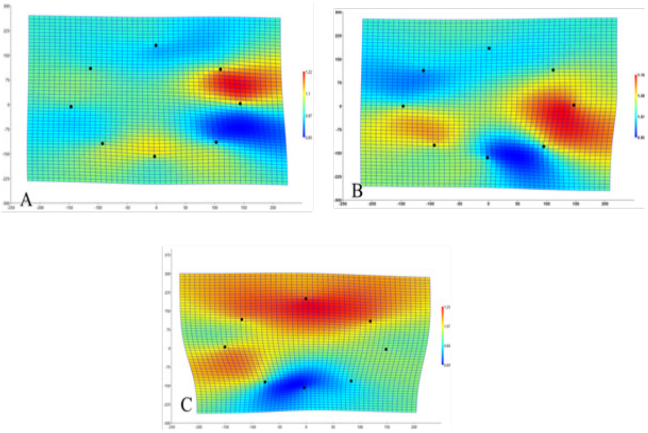

Figure 3. A) A thin-plate spline demonstrating the mean cranium shape deformation from 1 to 2 years old. The expansion factors on the landmarks are shown with colors; B) A thin-plate spline demonstrating the mean cranium shape deformation from the age of 2 to 3 years. The expansion factors at the landmarks are shown with colors; C) A thin-plate spline demonstrating the mean cranium shape deformation from the age of 3 to 4 years. The expansion factors at the landmarks are shown with colors.

Table 1. Definitions of landmarks used in the present study.

LN	Corpus callosum	Cranium
1	Anterior point of cc	Frontmost point of the craium
2	Interior notch of the splenium	The point at which the line that passes through the midpoint of the segment, which was drawn from landmark 1 to landmark 3
3	Inferior tip of the splenium	Coronal suture
4	Posterior-most point of the CC	Lambdoid suture
5	Top most point of the splenium	Backmost point of the cranium
6	Top most point of the CC	Lambdoid suture
7	Posterior angle of the genu	Coronal suture
8	Posterior tip of the genu	The point at which the line that passes through the midpoint of the segment, which was drawn from landmark 1 to landmark 7
9	The point at which the line that passes through landmark 7, is perpendicular to the segment, which was drawn from landmark 1 to landmark 7, and cuts the upper bound of the CC	
10	The point at which the line that passes through landmark 6, is perpendicular to the segment, which was drawn from landmark 5 to landmark 6, and cuts the lower bound of the CC	
11	The point at which the line that passes through the midpoint of the segment, which was drawn from landmark 5 to landmark 6, is perpendicular to this segment, and cuts the upper bound of the CC	
12	The point at which the line that passes through the midpoint of the segment, which was drawn from landmark 6 to landmark 9, is perpendicular to this segment, and cuts the lower bound of the CC	
13	The point at which the line that passes through the midpoint of the segment, which was drawn from landmark 6 to landmark 9, is perpendicular to this segment, and cuts the upper bound of the CC	
14	The point at which the line that passes through the midpoint of the segment, which was drawn from landmark 7 to landmark 12, is perpendicular to this segment, and cuts the lower bound of the CC	
15	The point at which the line that passes through landmark 7 and the midpoint of the segment, which was drawn from landmark 1 to landmark 8, and cuts the left boundary of the CC	
16	The point at which the line that passes through landmark 11 and the midpoint of the segment, which was drawn from landmark 2 to landmark 10, and cuts the lower bound of the CC	

characterized by widening in the dark red region and narrowing in the dark blue regions.

The average cranium shapes of the age groups are presented in Figure 2. In the analyses performed between consecutive age groups, the cranium shapes differed between 1-year-old and 2-year-old groups, 2-year-old and 3-year-old groups, and 3-year-old and 4-year-old groups ($p<0.001$, $p=0.047$, and $p<0.001$, respectively). However, no significant differences in this respect were observed between the 4-year-old and 5-year-old groups ($p=0.345$).

TPS analysis was also performed using mean cranium shapes of 1-year-old and two-year-old groups obtained from the Procrustes analysis. The TPS graphic shows high deformations in the shapes of the corpus callosum at the age of one to two years (Figure 3).

Enlargement was observed in the dark red region, and narrowing in the dark blue regions, while the highest deformation was found in the transition from one year to two years old. Figure 3 shows an enlargement in the dark red region and a narrowing in the dark blue regions during the transition from 2 to 3 years of age. In addition, Figure 3 shows an enlargement in the dark red region and a narrowing in the dark blue regions as the age increases from 3 to 4 years.

Discussion

In the present study, we aimed to investigate the association between age and structural deformation of the corpus callosum and cranium. We used the landmark-based geometrical morphometric approach to evaluate these changes. Our results showed significant changes in the corpus callosum and cranium shapes with the increase in age. Further subregional analyses revealed that the most prominent deformation was in the posterior midbody, the corpus callosum region containing callosal fibers that interconnect the somatosensory cortices. The most significant deformation in the cranium was observed in the biparietal area.

The relationship between brain morphology and function has been extensively studied [12,13]. A recent MRI study has determined the central sulcus's relations, functional body representations, and particular morphological features [14]. Sun et al. tested 252 right-handed subjects and confirmed a perfect match between the central sulcus morphological “hand knob” and the corresponding motor activation [15].

There is a more than 2-fold increase in the size of genu and splenium of the corpus callosum in the first year after birth [16]. While the growth of the genu is completed at the age of 5–6 years, the growth of the splenium and, consequently, the corpus callosum continues until the age of 10–12 years. Garel et al. reported that the genu expands more than the splenium during early development, and the splenium expands more during later development. They showed that the enlargement of the corpus callosum occurs from anterior to posterior during growth [17]. A later, longer-term expansion of the splenium compared with genu may indicate greater myelination in the splenial component [18].

Barkovich and Kjos performed an MRI study to evaluate the corpus callosum morphology in 63 patients aged < 1 year and found that it was uniformly thin without enlargements in the genu and splenium during the first postnatal year [19].

In their cross-sectional study using MRI, Giedd et al. found more age-related changes in the middle and posterior parts of the corpus callosum (body, splenium) than in the anterior parts (genu, rostrum) in individuals aged 4–18 years [20]. However, they did not evaluate the corpus callosum developments in children under < 4 years of age.

Therefore, they did not assess the period during which a maximum expansion of the corpus callosum occurs after birth.

The corpus callosum enlarges together with the growth of the cortex. In the early postnatal period, the maturation of the corpus callosum progresses with the development of myelin, especially at the splenium [21]. Myelination occurs from posterior to anterior; therefore, the primary cortical areas are connected to the isthmus and splenium. The body, genu, and rostrum are associated with more anterior associative regions [21].

Brain injury is associated with corpus callosum development and neurodevelopmental outcomes in premature infants. It reflects the severity of white matter injury and intraventricular hemorrhage [22].

Corpus callosum is related to the language functions of the splenium [6]. The splenium contains fibers projecting to primary visual cortices among additional cortical targets [5]. Because of this connectivity, splenium plays a vital role in orienting to salient information during infancy and adulthood [23]. The splenium may be a critical neurobiological region for emerging language production due to its role in maintaining visual orientation [24, 25]. The role of splenium in language has also been investigated in dyslectic adults.

In this study, we observed differences between the 1-year-old and 2-year-old groups with respect to corpus callosum shape. The rapid enlargement in the genu part of the corpus callosum during this period may be associated with infants' acquisition of speech ability. However, it is unclear whether learning to speak causes an enlargement in these fibers or whether enlargement in the fibers enables the acquisition of speaking ability.

Many researchers have compared the changes in corpus callosum structure between males and females; however, in this study, there were no significant between-group differences concerning gender distribution [16]. Assessment of sex-based differences was beyond the scope of this study

The head circumference has been shown to correlate with brain growth and brain volume. Head circumference measurements were associated with brain tissue volumes on MRI and neurocognitive outcomes in preterm infants compared with a head circumference at term equivalent age. MRI studies have also shown decreased fractional anisotropy in the splenium in premature infants with neurodevelopmental delay. A 3-dimensional study examining the growth of the cranium identified a non-uniform growth pattern. In our study, the diameter of the cranium increased up to 4 years old, which is consistent with the literature; however, this increase was not found to be uniform, especially in the biparietal areas. This suggests that the relationship established between skull diameter and neural development in the literature may not be entirely correct and that other factors may also affect neural development.

Limitation

We did not examine the sex-based differences in this study.

Conclusion

This study found that the growth in the skull and the development in the corpus callosum are not similar and that the development in the corpus callosum may be a better indicator of neural development than skull enlargement. More extensive studies, including clinical and radiological data, are required to understand this issue better.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical *standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

***Funding:** None*

Conflict of interest
The authors declare no conflict of interest.

References

1. Ercan I, Ocakoglu G, Sigirli D, Ozkaya G, Statistical shape analysis and usage in medical sciences. Turkiye Klinikleri J Biostat. 2012;4(1):27–35.
2. Bocu Y, Karabagli H, Taskapilioglu MÖ, Ocakoglu G. Statistical shape analyses of corpus callosum changes at preoperative and postoperative scaphocephaly patients. Childs Nerv Syst. 2022;38(4):773–80.
3. Ocakoglu G, Taskapilioglu MO, Kaya S, Yazici Z. Statistical shape analyses of patients with scaphocephaly after surgical remodeling. Turk Neurosurg. 2020;30(3):382–86.
4. Paul LK. Developmental malformation of the corpus callosum: a review of typical callosal development and examples of developmental disorders with callosal involvement. J Neurodev Disord. 2011;3(1):3–27.
5. Putnam MC, Steven MS, Doron KW, Riggall AC, Gazzaniga MS. Cortical projection topography of the human splenium: hemispheric asymmetry and individual differences. J Cogn Neurosci. 2010;22(8):1662–69.
6. Swanson MR, Wolff JJ, Elison JT, Gu H, Hazlett HC, Botteron K, et al. Splenium development and early spoken language in human infants. Dev Sci. 2017;20(2):10.1111/desc.12360.
7. Witelson SF. Hand and sex differences in the isthmus and genu of the human corpus callosum: a postmortem morphological study. Brain. 1989;112(3):799–835.
8. Sigirli D, Ercan I, Ozdemir ST, Taskapilioglu O, Hakyemez B, Turan OF. Shape analysis of the corpus callosum and cerebellum in female MS patients with different clinical phenotypes. Anat Rec. 2012;295(7):1202–11.
9. Dimitrov D. Reliability. In: Erford BT (editor). Assessment for Counselors. Boston: Houghton-Mifflin/Lahaska Press; 2006. p. 99–122.
10. Bookstein FL. Principal warps: thin-plate splines and the decomposition of deformations. IEEE Trans Pattern Anal Mach Intell. 1989;11(6):567–85.
11. Hammer Ø, Harper DAT, Ryan PD. PAST: paleontological statistics software package for education and data analysis. Palaeontol Electron. 2001;4:9.
12. Amiez C, Kostopoulos P, Champod AS, Petrides M. Local morphology predicts functional organization of the dorsal premotor region in the human brain. J Neurosci. 2006;26(10):2724–31.
13. Bodin C, Takerkart S, Belin P, Coulon O. Anatomo-functional correspondence in the superior temporal sulcus. Brain Struct Funct. 2018;223(1):221–32.
14. Germann J, Chakravarty MM, Collins DL, Petrides M. Tight coupling between morphological features of the central sulcus and somatomotor body representations: a combined anatomical and functional MRI study. Cereb Cortex. 2020;30(3):1843–1854.
15. Sun ZY, Pinel P, Rivière D, Moreno A, Dehaene S, Mangin JF. Linking morphological and functional variability in hand movement and silent reading. Brain Struct Funct. 2016;221(7):3361–71.
16. Vannucci RC, Barron TF, Lerro D, Antón SC, Vannucci SJ. Craniometric measures during development using MRI. NeuroImage. 2011;56(4):1855–64.
17. Garel C, Cont I, Alberti C, Josserand E, Moutard ML, Ducou le Pointe H. Biometry of the corpus callosum: MR imaging reference data. AJNR Am J Neuroradiol. 2011;32(8):1436–43.
18. Aboitiz F, Montiel J. One hundred million years of interhemispheric communication: the history of the corpus callosum. Braz J Med Biol Res. 2003;36(4):409–20.
19. Barkovich AJ, Kjos BO. Normal postnatal development of the corpus callosum as demonstrated by MR imaging. AJNR Am J Neuroradiol. 1988;9(3):487–91.
20. Giedd JN, Rumsey JM, Castellanos FX, Rajapakse JC, Kaysen D, Vaituzis AC, et al. A quantitative MRI study of the corpus callosum in children and adolescents. Brain Res Dev Brain Res. 1996;91(2):274–80.
21. Girard N, Koob M, Brunel H. Normal development. Handb Clin Neurol. 2016;136:1091–119.
22. Malavolti AM, Chau V, Brown-Lum M, Poskitt KJ, Brant R, Synnes A, et al. Association between corpus callosum development on magnetic resonance imaging and diffusion tensor imaging, and neurodevelopmental outcome in neonates born very preterm. Dev Med Child Neurol. 2017;59(4):433–40.
23. Elison JT, Paterson SJ, Wolff JJ, Reznick JS, Sasson NJ, Gu H, et al. White matter microstructure and atypical visual orienting in 7-month-olds at risk for autism. Am J Psychiatry. 2013;170(8):899–908.
24. Vouloumanos A, Curtin S. Foundational tuning: how infants' attention to speech predicts language development. Cogn Sci. 2014;38(8):1675–86.
25. Yapıcı-Eser H, Onay A, Öztop-Çakmak Ö, Egemen E, Vanlı-Yavuz EN, Solaroğlu İ. Rare case of glioblastoma multiforme located in posterior corpus callosum presenting with depressive symptoms and visual memory deficits. BMJ Case Rep. 2016; bcr2016216505 DOI: 10.1136/bcr-2016-216505.

How to cite this article:
***Duygu Baykal, Yaprak Çevirme, Gökhan Ocakoğlu, Mevlüt Özgur Taskapılıoğlu.** Development of the corpus callosum during normal growth. Ann Clin Anal Med 2023;14(9):844-848*

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